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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/820,530	04/07/2004	Dennis Benjamin	PPI-144	8326

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EXAMINER	
PERREIRA, MELISSA JEAN	
ART UNIT	**PAPER NUMBER**
1618	

MAIL DATE	DELIVERY MODE
08/19/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/820,530	BENJAMIN ET AL.	
	Examiner	Art Unit	
	MELISSA PERREIRA	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 June 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *6-13,16-18 and 26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *6-13,16 and 17* is/are rejected.

7)☐ Claim(s) *18 and 26* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 6-13,16-18 and 26 are pending in the application. Any objections and/or rejections from previous office actions that have not been reiterated in this office action are obviated.

Response to Arguments

1. Applicant's arguments filed 6/23/08 have been fully considered but they are not persuasive.

Claim Rejections - 35 USC § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

3. Claims 6-13,16 and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Turk et al. (*Chem. Biol.* **1999**, *6*, 823-833) in view of Soker et al. (US 2005/0112063A1) as stated in the office action mailed 12/21/07.

4. Applicant asserts that there is no teaching or suggestion in Turk et al. to administer a test compound to a subject or removing a plurality of biological samples from the subject.

5. The examiner concedes that Turk et al. does not teach of the administration of the fumagillin analog to a subject or removing biological samples from the subject. The reference of Turk et al. was not used to teach of the administration of the fumagillin

analog to a subject or removing biological samples from the subject but was used to teach the method of determining unbound MetAP2 via treatment of endothelial cells (in vitro) with TNP-470.

6. Applicant asserts that Soker et al. teaches that the bioeffectiveness of TNP-40, an anti-angiogenic compound, may be assessed by determining the amount of a protein in a single bodily fluid but fails to teach or suggest that the amount of free MetAP-2 is, or can be, determined in such a single bodily fluid. Applicant asserts that Soker et al. does not teach that inhibition of cell proliferation by the anti-angiogenic compound in a biological sample is correlated with the amount of free MetAP-2 in the biological sample or that removing a plurality of biological samples from the subject, wherein each of the plurality of biological samples is derived from a different tissue of the subject.

7. The reference of Soker et al. was used to teach that TNP-470 may be administered to a patient and that biological samples (blood, liver) may be subsequently removed. The reference of Turk et al. was used to teach that the determination of unbound MetAP2 is accomplished via treatment of endothelial cells (in vitro) with TNP-470. Also, it is known that TNP-470 is administered to a patient prior to biological sample removal (Soker et al) and that the determination of unbound MetAP2 is accomplished via examination of endothelial cells. Therefore it would have been obvious/predictable to one skilled in the art to remove endothelial cells from a patient post-administration of TNP-470 to determine the amount of unbound MetAP-2. The references of Turk et al. and Soker et al. are drawn to the use of the known anti-angiogenic compound, TNP-470, and therefore improving upon the known in vitro

technique of examining endothelial cells with TNP-470 for an in vivo method is predictable and obvious to try.

8. Claims 6-13,16 and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Griffiths et al. (*Proc. Natl. Acad. Sci.* **1998**, *95*, 15183-15188) in view of Soker et al. (US 2005/0112063A1) as stated in the office action mailed 12/21/07.

9. Applicant asserts that Griffiths et al. fails to teach administering a test compound to a subject or removing a plurality of biological samples from the subject, wherein each of the plurality of biological samples is derived from a different tissue of the subject.

10. The examiner concedes that Griffiths et al. does not teach of the administration of the fumagillin analog to a subject or removing biological samples from the subject. The reference of Griffiths et al. was used to teach in vitro binding of the fluorescein-fumagillin analog to the MetAP2. Also, TNP-470 is undergoing clinical trials for the treatment of a variety of cancers via inhibition of angiogenesis (inhibiting endothelial cell proliferation (abstract; p15183, paragraph 1).

11. Applicant asserts that Soker et al. teaches that the bioeffectiveness of TNP-40, an anti-angiogenic compound, may be assessed by determining the amount of a protein in a single bodily fluid but fails to teach or suggest that the amount of free MetAP-2 is, or can be, determined in such a single bodily fluid. Applicant asserts that Soker et al. does not teach that inhibition of cell proliferation by the anti-angiogenic compound in a biological sample is correlated with the amount of free MetAP-2 in the biological sample

or that removing a plurality of biological samples from the subject, wherein each of the plurality of biological samples is derived from a different tissue of the subject.

12. The reference of Soker et al. was used to teach that TNP-470 may be administered to a patient and that biological samples (blood, liver) may be subsequently removed. The reference of Griffiths et al. was used to teach in vitro binding of the fluorescein-fumagillin analog to the MetAP2. It is known that TNP-470 is administered to a patient prior to biological sample removal (Soker et al) and that the determination of unbound MetAP2 via examination of recombinant human MetAP2 is predictable. Therefore it would have been obvious/predictable to one skilled in the art to remove cells, such as cancer cells (Griffiths et al.) from a patient post-administration of TNP-470 to determine the amount of unbound MetAP-2. The references of Griffiths et al. and Soker et al. are drawn to the use of the known fumagillin analogs and therefore improving upon the known in vitro technique of examining a sample for an in vivo method is predictable and obvious to try.

13. Applicant asserts that Soker et al. fails to teach or suggest that the excised liver is, or may be, used to determine the amount of free anti-angiogenic compound in the single biological sample or that a plurality of biological samples from the subject, wherein each of the plurality of biological samples is derived from a different tissue of the subject.

14. The reference of Soker et al. was used to teach that TNP-470 may be administered to a patient and that biological samples (blood, liver) may be subsequently removed and not used to teach of determining the amount of free anti-angiogenic

compound in the single biological sample. The reference of Griffiths et al. was used to teach in vitro binding of the fluorescein-fumagillin analog to the MetAP2. It is known that TNP-470 is administered to a patient prior to biological sample removal (Soker et al) and that the determination of unbound MetAP2 via examination of recombinant human MetAP2 is predictable. Therefore it would have been obvious/predictable to one skilled in the art to remove cells, such as cancer cells (Griffiths et al.) from a patient post-administration of TNP-470 to determine the amount of unbound MetAP-2. The references of Griffiths et al. and Soker et al. are drawn to the use of the known fumagillin analogs and therefore improving upon the known in vitro technique of examining a sample for an in vivo method is predictable and obvious to try.

Conclusion

No claims are allowed at this time. Claim 18 is objected to for depending on a rejected claim and claim 26 is free of the prior art.

15. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MELISSA PERREIRA whose telephone number is (571)272-1354. The examiner can normally be reached on 9am-5pm M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mike Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michael G. Hartley/
Supervisory Patent Examiner, Art Unit 1618

/Melissa Perreira/
Examiner, Art Unit 1618

Application Number	Application/Control No.	Applicant(s)/Patent under Reexamination	
	10/820,530	BENJAMIN ET AL.	
	Examiner	Art Unit	
	MELISSA PERREIRA	1618	